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Article

Knowledge and Prevalence of Latent Tuberculosis Infection: A Pilot Study in Patients Attending a Primary Healthcare Clinic in Rural Eastern Cape, South Africa

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Abstract: Latent tuberculosis infection (LTBI) remains a significant global health concern, particularly in regions with high tuberculosis (TB) prevalence, such as South Africa. This pilot study aimed to evaluate the prevalence of LTBI and assess patient knowledge about the condition in a primary healthcare clinic in rural Eastern Cape, South Africa. A cross-sectional design was used, and convenience sampling recruited outpatients aged 18 years and older with no prior history of TB. Blood samples were analyzed using the QuantiFERON-TB Gold assay to determine LTBI status, and a survey assessed patient knowledge of LTBI. Strong positive correlations were observed between what patients understand by the term LTBI and how is LTBI different from TB (0.70), patients understand by the term LTBI and the risk factors for developing LTBI (0.70), how is LTBI different from TB and the risk factors for developing LTBI (0.78), and how is LTBI different from TB and the recommended treatments for LTBI (0.79), indicating overlap in understanding. In contrast, negative correlations between if patients ever heard of latent LTBI before and patients understanding the term LTBI (-0.25), the risk factors for developing LTBI (-0.22), LTBI progressing to active TB (-0.27), and the recommended treatments for LTBI (-0.27). This divergence points to different dimensions of patient knowledge and awareness. Age, gender, occupation, comorbidities, and HIV status showed varying LTBI positivity trends. Among younger patients aged 20-29, 15.4% tested positive, while the 30-39 group showed a nearly equal split between positive (48.1%) and negative cases. A higher positivity rate was seen in females (39.1%) compared to males (31.6%). Unemployed individuals had higher positivity rates, suggesting socioeconomic factors' influence. Comorbidities, especially hypertension, diabetes, and asthma, correlated with higher LTBI positivity among females, but this was less evident in males. HIV-positive patients had a higher LTBI-negative rate compared to HIV-negative patients. These findings suggest that demographic and health factors, including age, gender, occupation, comorbidities, and HIV status, may predict LTBI positivity.

Keywords: latent tuberculosis infection; knowledge; prevalence; comorbidities; gender; age; education

1. Introduction

Latent Tuberculosis Infection (LTBI) is a state where individuals are infected with *Mycobacterium tuberculosis* but do not exhibit symptoms of active TB. The global burden of LTBI is substantial, with an estimated one-quarter of the world's population affected, particularly in regions with high tuberculosis (TB) incidence, such as South Africa [1]. Detecting LTBI early is crucial for the World Health Organization's End Tuberculosis Strategy [2]. *Mycobacterium tuberculosis* (*Mtb*) poses a significant threat to public health worldwide, with 10 million people developing TB and 1.6 million succumbing to it annually. *Mtb* has shared a long evolutionary history with humans, exerting its influence over millennia [3]. One key factor contributing to its effectiveness as a pathogen lies in its capacity to reside within its host without causing symptoms, entering a dormant state known as

latency [3]. Later, in minority of cases, it can progress to active TB after months or even years of dormancy. The likelihood of LTBI reactivating into TB disease during a person's lifetime varies depending on their age at the time of infection and the presence of any additional medical conditions associated with TB progression [3]. Tuberculosis infections can manifest as active TB (ATBI), LTBI or other nontuberculous mycobacterial infection (NTM) [4]. The majority of individuals who are exposed to *Mtb* develop LTBI and remain susceptible to progressing to active TB (VanValkenburg et al., 2022). While most TB patients have LTBI, only a small percentage, about 5–15%, develops symptomatic illness. However, individuals with active infection face the risk of reactivation even after completing treatment. Therefore, diagnosing LTBI is critical in TB management to prevent its progression to active TB [5].

Tuberculosis remains a significant contributor to global mortality from infectious diseases, despite the availability of effective treatment and prevention methods for both active and latent TB [6–9]. This means that a large proportion of TB-related deaths could be avoided. With approximately one quarter of the world's population harboring LTBI, it serves as a reservoir for the initiation of new TB cases [10]. Many of the world's population carry the *Mtb* infection with the majority displaying no tuberculosis disease symptoms and posing no infectious risk [11]. Nonetheless, these individuals are still vulnerable to developing active TB disease and potentially becoming contagious [12].

Demographic factors such as gender and socioeconomic status also play a role in LTBI prevalence across age groups. For instance, a study in England found that LTBI positivity was higher among older migrants, with rates ranging from 25% to 30% in various studies [13]. Additionally, healthcare workers, particularly those born outside the country, showed elevated LTBI rates, emphasizing the intersection of age, occupation, and migration status [14,15].

The relationship between occupational exposure and the prevalence of LTBI is well-documented, particularly among healthcare workers (HCWs) and other high-risk occupational groups. Various studies have consistently shown that individuals working in healthcare settings, especially those with direct patient contact, exhibit significantly higher rates of LTBI compared to those in other professions. Healthcare workers, particularly nurses and medical staff, are at an elevated risk for LTBI due to their frequent exposure to patients with active TB. A systematic review indicated that HCWs who have more direct contact with TB patients or prolonged exposure are significantly more likely to test positive for LTBI [16]. The findings from a study in South Africa, highlighted that specific work locations, such as TB wards and outpatient departments, are associated with increased risk of both active TB disease and LTBI among healthcare personnel [17]. Another study in China found that the prevalence of LTBI was markedly higher in high-risk workplaces (37.4%) compared to low-risk environments (29.8%) [18].

Understanding the prevalence of LTBI and the knowledge surrounding it in our study setting that is burdened with TB is crucial for effective public health strategies aimed at TB control.

2. Materials and Methods

This pilot study was a cross-sectional study conducted at a primary healthcare clinic in rural Eastern Cape, South Africa. Convenience sampling was used to recruit 88 outpatients following inclusion criteria of age 18 years or older with no history of TB infection and exclusion criteria of confirmed or probable active TB and receipt of anti-tuberculosis treatment. Patients who consented to be participants of the study were surveyed regarding their knowledge of LTBI following questions on Table 1 and underwent blood collection by QuantiFERON-TB Gold blood collection tubes for testing the prevalence of LTBI. Study participants blood samples were tested by QFTGIT assay kits from Cellestis Limited, Australia, following the protocol outlined by the manufacturer [19,20] to assess presence of LTBI. Optical density readings were recorded using a micro plate reader equipped with 450- and 620-nm filters (Molecular Devices Corporation, USA). The QuantiFERON-TB Gold Analysis Software (Cellestis Limited) was used to analyze results. Python version 3.8. and R version 4.1.1 software were used to analyze date and a $p < 0.05$ was considered to be significant.

Table 1. Knowledge of LTBI survey questions.

Question code	Question
Q1	Have you ever heard of latent tuberculosis infection (LTBI) before?
Q2	Have you ever received health education on LTBI and TB?
Q3	What do you understand by the term “latent tuberculosis infection”?
Q4	How is LTBI different from active tuberculosis (TB)?
Q5	What are the risk factors for developing LTBI?
Q6	What are the possible consequences of having untreated LTBI?
Q7	Can LTBI progress to active TB?
Q8	What are the recommended treatments for LTBI?
Q9	Are there any preventive measures individuals with LTBI should take to avoid developing active TB?
Q10	Do you think LTBI is a significant public health concern?
Q11	How concerned are you about the possibility of progressing from LTBI to active TB?
Q12	Do you believe that LTBI treatment is necessary, even if you do not have symptoms?
Q13	How do you perceive the importance of LTBI screening programs?
Q14	What barriers do you think may prevent individuals from seeking LTBI testing or treatment?
Q15	Have you ever been screened for LTBI?
Q16	If you tested for LTBI, did you receive treatment?
Q17	If you received treatment for LTBI, did you complete the entire course of medication?

Q18	Have you ever been in close contact with someone diagnosed with active TB?
Q19	If yes, did you seek medical evaluation or testing for LTBI?

3. Results

In Figure 1 a strong positive, weak and strong negative correlations of knowledge were observed. Q3 and Q4 (0.70) indicates that patients responses to Q3 are highly similar to their responses to Q4, suggesting that these questions address closely related concepts. Q3 and Q5 (0.70) further highlights the similarity in responses, implying that these questions capture overlapping knowledge or attitudes. Q4 and Q5 (0.78) suggest stronger correlation and indicating that these questions are likely assessing the same or very closely related constructs. Q4 and Q8 (0.79) suggests that patients provided aligned answers, pointing to a shared understanding. Q3 and Q8 (0.73) is reinforcing the idea that these questions reflect related knowledge or perceptions. Q1 and Q8 (-0.27) indicates a weak to moderate negative correlation suggesting an inverse relationship in how patients answered these questions, possibly indicating that knowledge or attitudes measured by Q1 differ from those captured by Q8. Q1 and Q5 (-0.22) suggest that participants who scored higher on Q1 tend to score lower on Q5, though the relationship is not strong. Q1 and Q3 (-0.25) suggests a potential divergence in knowledge or attitudes between these questions. Q1 and Q7 (-0.27) indicates that higher scores on Q1 may be associated with lower scores on Q7, pointing to a contrast in understanding between these questions.

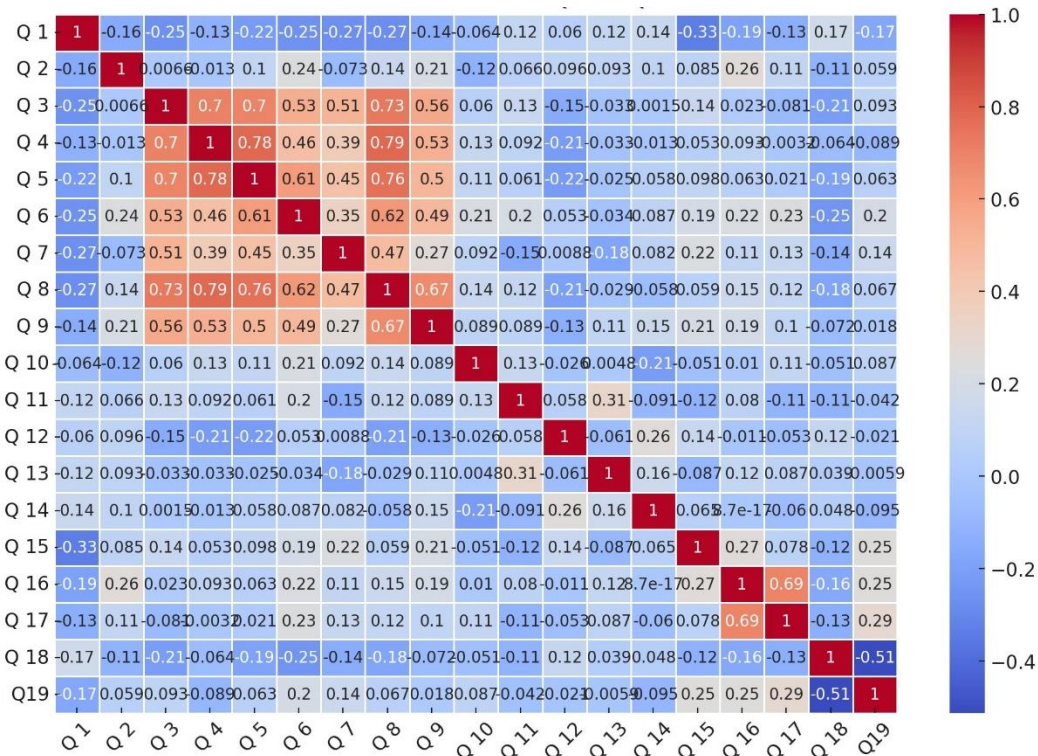


Figure 1. Correlation matrix for knowledge questions (Q1 To Q19).

The distribution of LTBI results by age group shows varying levels of positivity and negativity across different age ranges. The majority of patients (20-29 years) tested negative, with 84.6% negative and 15.4% positive. The results of patients (30-39 years) were more evenly split, with 51.9% negative and 48.1% positive. A slightly higher proportion of patients (40-49 years) tested negative, with 58.8%

negative and 41.2% positive. The patients (50-59 years) were similar to the 40-49 group, with 55.6% negative and 44.4% positive. A higher percentage of patients (60-69 years) tested negative, with 70.0% negative and 30.0% positive. All patients (70-79 years) tested negative, with 100% negative and 0% positive (Figure 2).

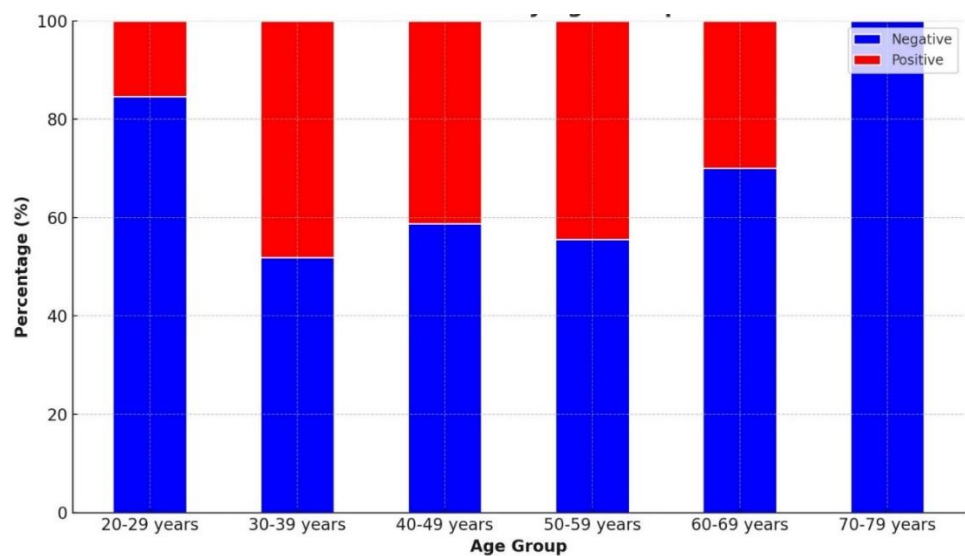


Figure 2. LTBI results by age group.

Figure 3 indicates a slightly higher rate of positivity among females (60.9% negative and 39.1% positive) compared to males (68.4% negative and 31.6% positive).

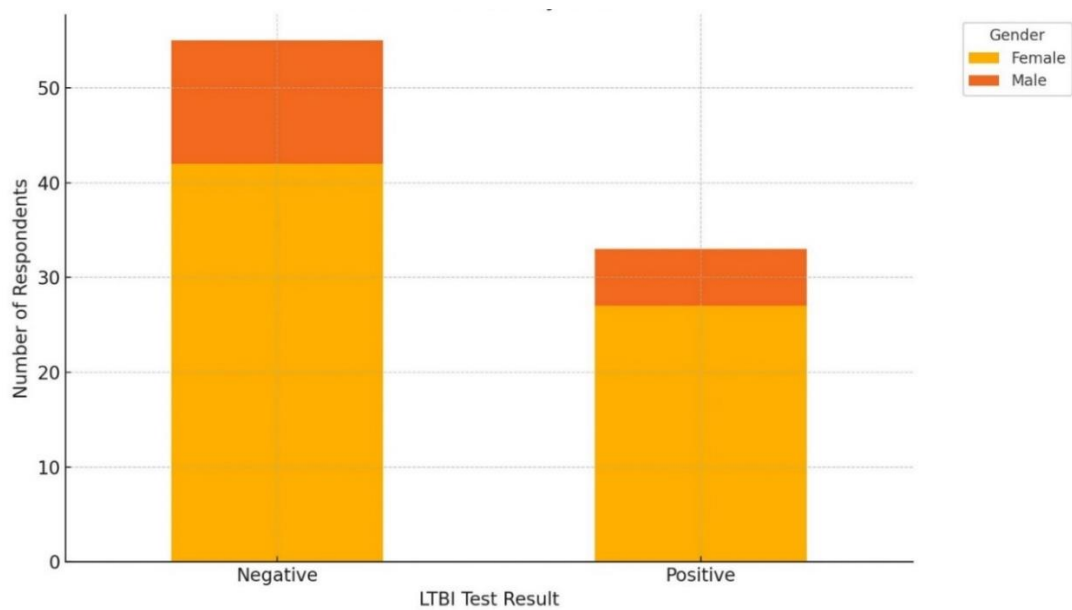


Figure 3. LTBI test results by gender.

Figure 4 compares LTBI test results by occupation providing insight into the relationship between different job categories and LTBI outcomes.

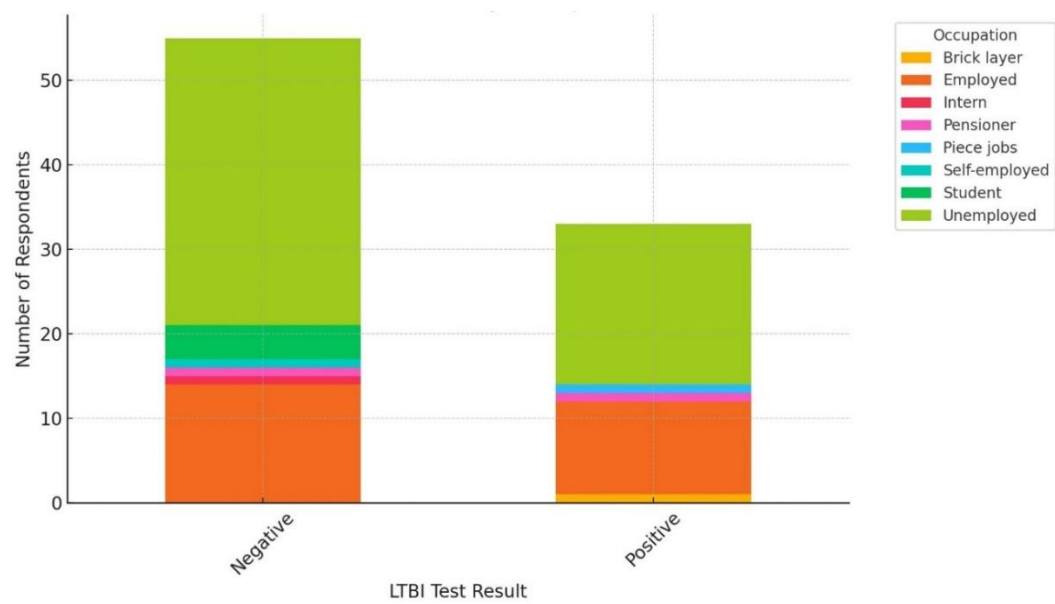


Figure 4. LTBI test results by occupation.

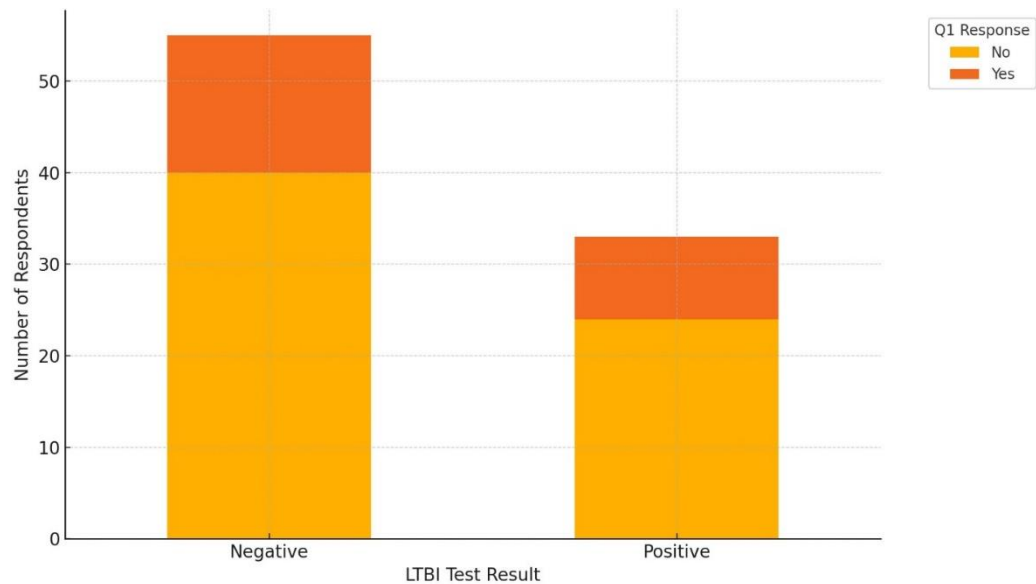


Figure 5. LTBI results by Q1 response.

Figure 6 compares Q1 responses across different education levels provides insights into how educational background may influence participants' views or knowledge related to the question posed in Q1.

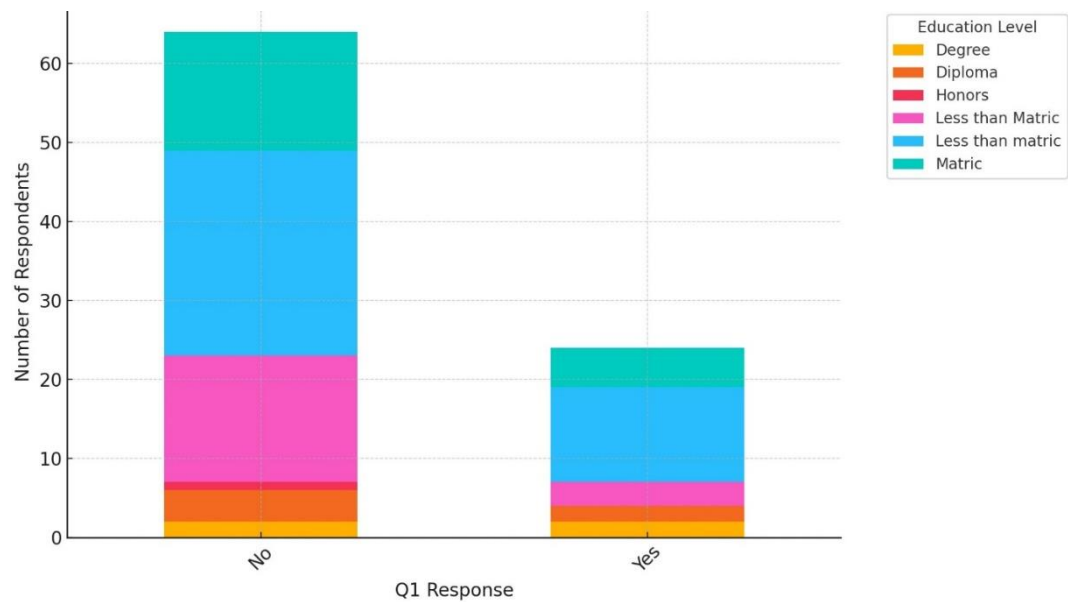


Figure 6. Q1 responses by education level.

Patients with hypertension had ten LTBI negative and five LTBI positive results which is the highest number of both positive and negative LTBI test results in the study. Patients with hypertension had a significant portion (33%) of those who tested positive. This suggests that hypertension may be a notable risk factor for LTBI positivity. There was one patient with both hypertension and asthma and one diabetic patient who tested positive for LTBI. Although the sample size is small, this suggests that comorbidities like diabetes and asthma combined with hypertension might be associated with an increased risk of LTBI positivity. Only one person with both diabetes and hypertension tested negative, which suggests that while these conditions are prevalent, they may not always coincide with LTBI positivity in this dataset. There is only one case of epilepsy with a negative result. This suggests that epilepsy alone, may not have a strong association with LTBI positivity (Figure 7).

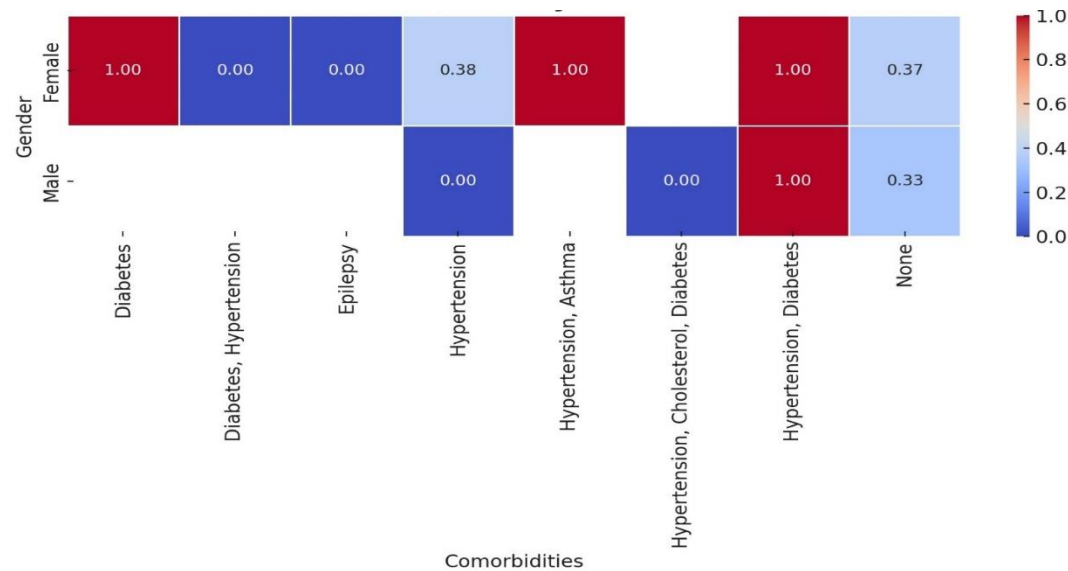


Figure 7. Correlation of LTBI test results by gender and comorbidities.

In females diabetes and hypertension with asthma comorbidities show a high correlation with LTBI positivity, with values close to 1 (100% positivity rate). This suggests that females with these conditions are more likely to test positive for LTBI. Females with hypertension show a moderate

positivity rate of about 38.5%. This suggests that hypertension alone is a somewhat moderate risk factor for LTBI positivity in females. There is limited data for males with certain comorbidities, such as diabetes and hypertension with asthma. The only significant data for males was in the category of none and hypertension, diabetes, showing some correlation with positivity rates. Epilepsy and diabetes with hypertension in females show no LTBI positivity (correlation of 0). This may indicate that patients in these groups are less likely to have. These patterns suggest that comorbidities like diabetes and hypertension, especially in combination, might be significant factors in predicting LTBI positivity among female. The bars' lengths visually emphasize the relative importance of each comorbidity. Diabetes has the highest importance, with a value approaching 0.200, meaning it is the most significant comorbidity. Hypertension, Asthma and Hypertension, Diabetes follow, with moderately high importance values around 0.150. Hypertension, None, and Epilepsy have lower importance, with values closer to 0.100. Diabetes, Hypertension (the combination of these two conditions listed separately) has the lowest importance, with a value near zero (Figure 8).

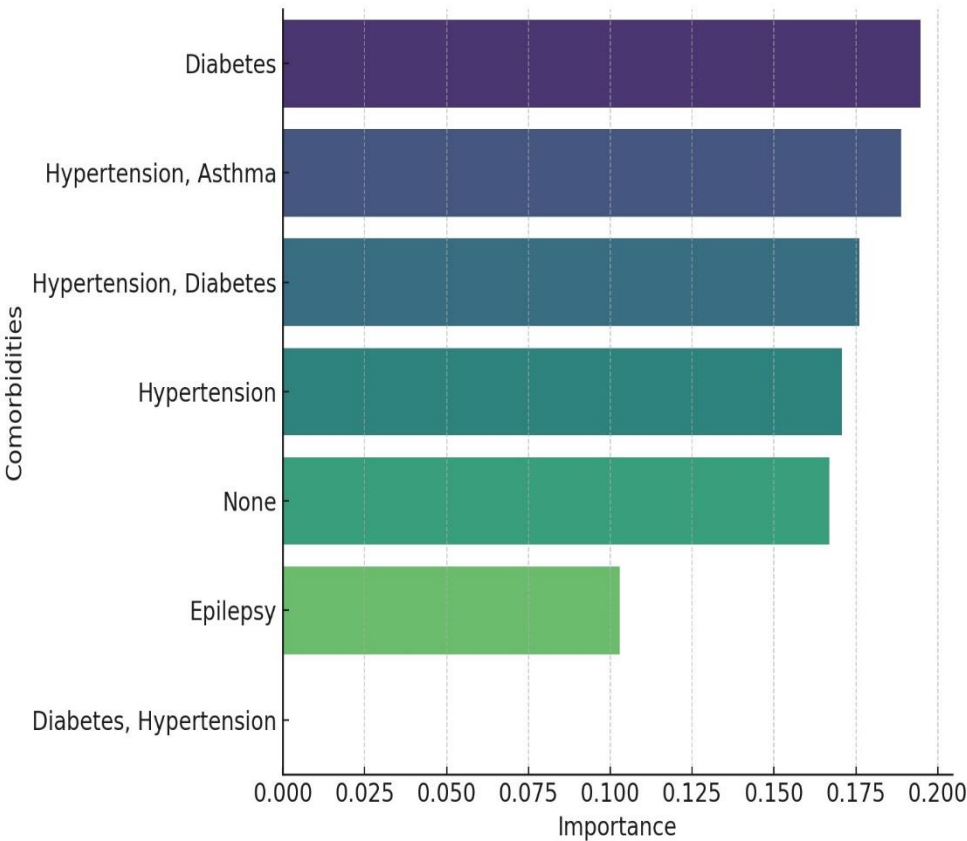


Figure 8. Feature importance for LTBI prediction.

The heatmap is comparing LTBI test results and HIV status offers insights into the relationship between these two health outcomes. Top left (24) represents patients who are HIV negative and had a negative LTBI test. Top right (31) represents individuals who are HIV positive and had a negative LTBI test. Bottom left (12) represents individuals who are HIV negative and had a positive LTBI test. Bottom right (21) represents individuals who are HIV positive and had a positive LTBI test. These results suggest a relationship between HIV status and LTBI test results. There are slightly more individuals with a negative LTBI result among HIV-positive people compared to HIV-negative ones (Figure 9).

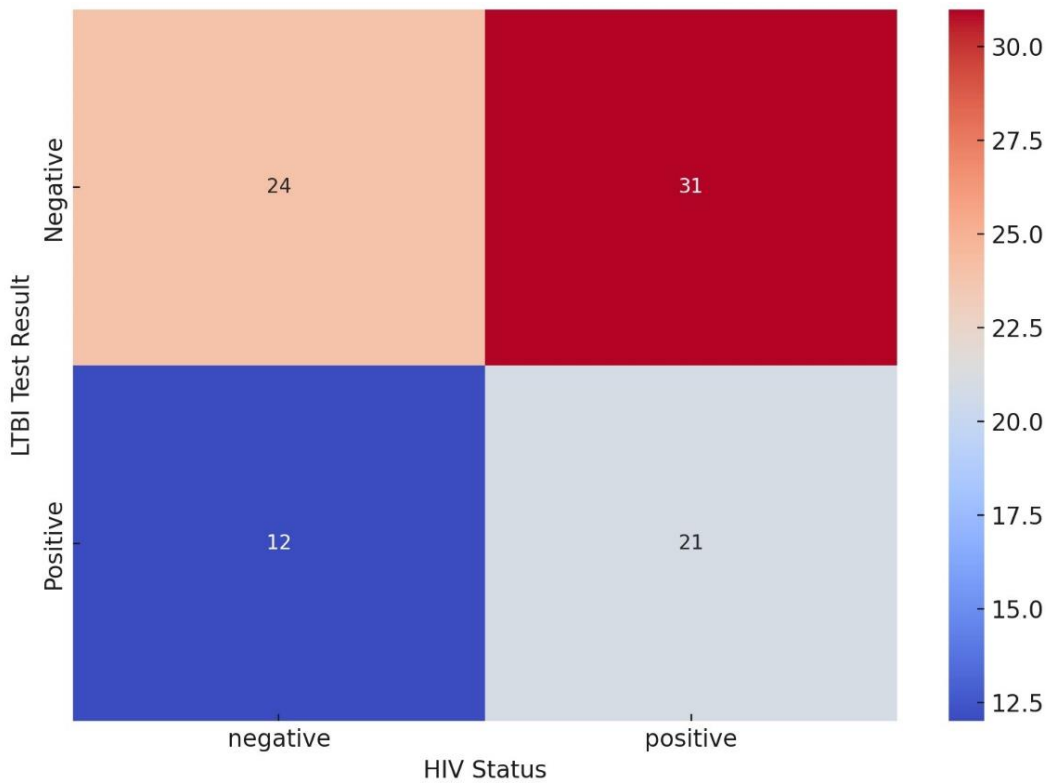


Figure 9. Correlation between LTBI test and HIV status.

4. Discussion

Tuberculosis remains a significant global health challenge, with an estimated 1.5 million deaths attributed to the disease in 2020 [21]. The identification of LTBI is crucial in controlling TB transmission, as individuals with LTBI are at risk of developing active TB. Understanding the demographic factors influencing LTBI-negative results can inform public health strategies aimed at reducing TB incidence.

The correlation matrix suggests that patients exhibit consistent knowledge in certain areas (e.g., specific risk factors or prevention strategies), but there are notable gaps between general awareness and more detailed, practical knowledge. Our study reveals two different levels of knowledge, foundational (Q1) and more advanced, specific knowledge (Q3-Q8). Patients seem to either possess one or the other, but not consistently both. The weaker correlations between Q1 and Q11-Q12 suggest that general knowledge does not always translate into concern or understanding of practical barriers. There is a gap between general knowledge and behavior-related knowledge, such as understanding preventive measures or risk factors. There is a divergence between general knowledge and more specific or advanced knowledge observed in our study. Patients who have some basic awareness do not have detailed or accurate knowledge about more complex information. Some studies indicate that individuals with higher levels of education tend to have a better understanding of LTBI and its associated risks, [22] found that improved education correlates with a reduction in LTBI risk, as individuals become more aware of health risks linked to lifestyle choices and environmental factors such as poverty and overcrowding [22]. Similarly, Gao et al. highlighted that many respondents in their study had low TB knowledge, often confusing LTBI with active TB disease, which can lead to misconceptions about the necessity of treatment [23]. This confusion underscores the need for targeted educational materials that accurately convey information about LTBI, its transmission, and treatment options [23].

In LTBI-Negative patients certain age groups, such as older or younger groups, showed a higher proportion of LTBI-negative results, indicating lower risk or exposure to TB, while younger age groups (e.g., 20-29, 30-39) had more LTBI-negative results which may suggest that these patients have better access to preventive healthcare or live in less risky environments. Older adults, particularly

those over 65 years, often show a higher proportion of LTBI-negative results, which may reflect a combination of factors including decreased exposure to TB due to improved living conditions and healthcare access over time [24]. Socioeconomic factors play a role in younger patients which is a benefit from improved living conditions and education about TB prevention [25]. The age groups of LTBI-Positive patients with a higher proportion of LTBI-positive results may indicate that older individuals or those within specific age ranges are more vulnerable to TB [25]. A higher count of LTBI-positive results in older groups could suggest accumulated exposure over time or reduced immunity as individuals age. Older adults often have a longer exposure history to TB, which can lead to a higher likelihood of LTBI positivity. Several studies have documented that individuals who have lived in areas with high TB prevalence or have had close contact with infectious TB cases are at increased risk of developing LTBI [24]. Historically, older adults may have been exposed to TB before the advent of effective public health measures, such as vaccination and improved sanitation. This accumulated exposure can result in a higher prevalence of LTBI in this demographic [26].

There is an age-specific risk observed in our study, as individuals age, their immune systems undergo changes that can affect their ability to control latent infections. The decline in immune function, often referred to as immunosenescence, can lead to an increased risk of LTBI positivity and progression to active TB disease. Research indicates that older adults may have a diminished immune response to *Mtb*, making it more challenging for their bodies to contain the infection. This reduced immune efficacy can result in a higher likelihood of LTBI positivity [27]. Older adults often present with comorbidities that can further compromise immune function, such as diabetes, chronic lung disease, and malignancies. These conditions can increase susceptibility to TB infection and may contribute to the higher rates of LTBI positivity observed in older populations [28]. The analysis reveals a clear trend in LTBI positivity rates across age groups. Younger individuals (20-29 years) exhibit the lowest rates of positivity, while older age groups (30-39 years and above) show increasing positivity rates. The findings reflect various factors, including historical exposure to TB, changes in public health policies, and variations in immune response related to age [29]. The absence of positive results in the 70-79 age group warrants further investigation. It may indicate effective public health interventions over the years or a demographic shift in exposure patterns [30]. Focused screening and preventive measures should be considered for age groups with higher positivity rates, particularly those aged 30-59.

Previous studies have shown that populations with limited access to health education often have lower awareness of LTBI, which can lead to higher rates of progression to active TB [1,31]. In a related context, a systematic review indicated that LTBI prevalence rates can be particularly high in vulnerable populations, such as refugees and asylum seekers, where rates were reported as high as 23% [31]. This aligns with findings from other studies in similar settings, suggesting that rural populations in South Africa may exhibit comparable or higher prevalence rates due to socioeconomic factors and healthcare access issues [32,33].

The findings from this pilot study highlight the urgent need for improved education and awareness regarding LTBI among patients in rural Eastern Cape. The lack of knowledge about LTBI can hinder early detection and treatment, increasing the risk of progression to active TB, which remains a leading cause of morbidity and mortality in South Africa [1,32]. Moreover, the high prevalence of LTBI reported in this study is consistent with global trends, where populations characterized by socioeconomic challenges often show elevated rates of LTBI [34]. For instance, studies have documented LTBI prevalence rates among healthcare workers and other high-risk groups, emphasizing the need for focused screening and preventive measures [35].

The distribution of LTBI-negative and LTBI-positive patients by occupation provides insight into the potential risk factors for TB exposure. Occupations with a higher proportion of LTBI-negative patients suggest lower TB exposure risks, potentially due to better job conditions, access to healthcare, or preventive measures [36]. Conversely, occupations with higher LTBI-positive rates, such as unemployment, indicated increased vulnerability due to factors like poor living conditions, limited healthcare access, or working in environments with higher TB exposure risks [37]. These findings highlight the importance of occupational and socioeconomic factors in TB prevention

Education plays a crucial role in shaping individuals' knowledge and awareness of health issues, including LTBI. Our results indicate that patients with higher education levels tend to have better health literacy, which is essential for understanding complex health issues such as LTBI. Higher education often correlates with increased access to information and resources, enabling individuals to make informed health decisions [38]. Responses to Q1 by education level suggest that patients with higher education (e.g., matric or beyond) have a preference for certain responses, indicating that education could influence knowledge or awareness of LTBI knowledge. Lower education levels exhibit different response patterns compared to higher education levels, which is highlighting gaps in understanding or awareness based on education [39]. Our findings reveal that educational attainment shapes perspectives on the issue. Higher education may correlate with more informed or specific responses, while lower education levels could indicate a need for more targeted information or awareness campaigns. A study by [38] indicated that educated individuals were more aware of the risks associated with untreated LTBI, leading to a higher likelihood of seeking treatment.

Hypertension, either alone or in combination with other conditions like asthma or diabetes, seems to be the most significant factor associated with LTBI positivity in our study. This suggests that patients with hypertension should be closely monitored for LTBI, especially if they have additional comorbidities. Hypertension may impair immune function, potentially increasing susceptibility to infections, including LTBI. For instance, elevated blood pressure has been associated with altered immune responses, which could hinder the body's ability to control latent infections [38]. The presence of hypertension in conjunction with other chronic conditions, such as asthma and diabetes, further complicates the risk profile for LTBI. [40] findings shown that individuals with multiple comorbidities are at a higher risk for LTBI positivity due to compounded effects on immune function and overall health. Our findings underscore the importance of considering multiple comorbidities when assessing LTBI risk.

A combination of LTBI-negative and HIV-negative had a high count suggesting that a significant portion of the patients are free from both LTBI and HIV, which may reflect a lower overall health risk in this group. A notable number in of LTBI-positive and HIV-negative might patients indicates that patients who are free from HIV could still be susceptible to LTBI, suggesting that the two conditions do not necessarily occur together. The coexistence of LTBI and HIV is a well-documented phenomenon, with HIV significantly increasing the risk of progression from LTBI to active TB [41]. However, a notable number of LTBI-positive patients may be HIV-negative, indicating that individuals without HIV can still be susceptible to LTBI. Several factors contribute to LTBI susceptibility in HIV-negative individuals, including socioeconomic status, living conditions, and occupational exposure. Individuals living in crowded or poorly ventilated environments are at increased risk of TB exposure, regardless of their HIV status [40]. Additionally, certain occupations, such as healthcare work, can increase the likelihood of LTBI positivity among HIV-negative individuals [40]. The combination of LTBI-Negative and HIV-Positive had a significant count, suggesting that patients with HIV may not always have LTBI, indicating that effective treatments or interventions might be limiting co-infections in this group. A higher number LTBI-Positive and HIV-Positive points to a potential correlation between LTBI and HIV, where individuals with HIV may be at increased risk of developing LTBI due to weakened immune systems or overlapping risk factors [26]. Our study reveals that co-occurrence of LTBI-positive and HIV-positive group patients with HIV are more prone to LTBI infections. Some studies found that patient with HIV are at an increased risk of LTBI due to several factors, including immune system compromise and shared risk factors for both infections [42]. HIV infection leads to a progressive decline in CD4⁺ T cells, which are crucial for controlling *M. tuberculosis* infection. Studies have shown that HIV-positive individuals exhibit a higher prevalence of LTBI, as their weakened immune systems are less capable of containing latent infections [38]. The notable Health Risk Patterns in our study reveals that lower numbers in LTBI-positive groups for HIV-negative patients could indicate that LTBI is more closely related to specific vulnerabilities or conditions like HIV. The notable presence of LTBI-positive patients who are HIV-negative indicates that susceptibility to LTBI is not limited to patients with HIV.

Hypertension shows the highest importance in predicting LTBI positivity, suggesting that hypertension is a significant factor in determining whether a female is likely to test positive for LTBI. The absence of comorbidities is the second most important factor, suggesting that the lack of any comorbid condition might still influence LTBI results, likely in relation to the general health profile of the patients without additional health burdens. The combination of hypertension and diabetes also contributes notably to LTBI prediction, highlighting that when these two conditions coexist, they become a stronger predictor for LTBI positivity than either condition alone. Diabetes on its own ranks lower in importance compared to hypertension or the combination of conditions. However, it still plays a significant role in the over-all prediction, indicating that diabetes could be a moderate risk factor for LTBI. Combination of hypertension and asthma also showed some contribution, though less important than hypertension alone or combined with diabetes, this may suggest that asthma does not add as much predictive power when coupled with hypertension. Epilepsy, Diabetes with Hypertension, have low or no impact in the model, indicating that they might not be strong predictors for LTBI positivity.

5. Conclusions

This pilot study highlights the significant burden of LTBI in a rural clinic population in the Eastern Cape, South Africa, and underscores the crucial role of early diagnosis and public health education in controlling TB transmission. In our study correlation analysis suggests that patients exhibit consistent, clustered knowledge in certain areas, while showing gaps between general awareness and more specific, actionable knowledge. There is a need focus on both increasing foundational knowledge and providing detailed, practical information can help bridge the divide between awareness and effective health behavior. Our findings reveal that LTBI prevalence varies across different demographic groups, with younger age groups showing lower LTBI positivity rates, potentially due to better access to preventive healthcare. In contrast, older adults and patients with comorbid conditions, such as hypertension, asthma, and diabetes, demonstrated higher rates of LTBI positivity, particularly among female patients. These results suggest that comorbid conditions, especially hypertension, may serve as key predictors of LTBI positivity, warranting close monitoring and preventive interventions for at-risk populations. The study also identified notable gaps in knowledge about LTBI, particularly among individuals with lower educational attainment. This highlights the need for focused public health initiatives to improve awareness and understanding of LTBI in rural and underserved communities. Addressing these knowledge gaps is essential for empowering community to seek timely care and treatment, ultimately reducing the progression from LTBI to active TB. Our study provides important information into the epidemiology of LTBI in a high-burden TB region and underscores the importance of integrating LTBI screening and education into routine healthcare services. Further large-scale studies are needed to confirm our findings and guide the development of focused interventions aimed at reducing TB incidence and mortality in rural South African settings.

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Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Data Availability Statement: Data can be requested from the corresponding author.

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Conflicts of Interest: The authors declare no conflicts of interest.

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